REMARKS

Applicants request reconsideration in light of the above amendments and following comments submitted under 37 C.F.R. § 1.111.

1. Status of the Claims

The status of the claims following entry of the amendments is as follows:

Claims pending: 17-21, 24-28, 31, and 47-48

Claims canceled: 1-16, 22-23, 29-30, and 32-46

Claims rejected: 17-32 and 47-48

Claims amended: 17, 24, and 47-48

2. Support for the Amendments

Applicants amend claims 17, 24, and 47-48 to more precisely recite the claimed subject matter. Support for the amendments can be found at least from (1) claims 23 and 30 (now canceled) and (2) the previously presented claims. Applicants do not believe that the amendments add prohibited subject matter that is unsupported by the Specification as filed.

The claims have been amended without prejudice to, or disclaimer of, the canceled subject matter. Applicants reserve the right to file a continuation or divisional application on any subject matter canceled by way of amendments.

3. Information Disclosure Statement

Applicants appreciate the Office's acknowledgement of the Information Disclosure Statement (IDS) submitted August 3, 2010.

Applicants submit herewith another IDS for consideration by the Office. Acknowledgement and return with the Office's next communication is respectfully requested.

4. The Application is "Special"

The present application has been pending over five years and is up for a third or subsequent Office Action. M.P.E.P. § 707.02 (Applications Up for Third Action and 5-Year Applications) states:

> The supervisory patent examiners are expected to personally check on the pendency of every application which is up for the third or subsequent Office action with a view to finally concluding its prosecution.
>
> Any application that has been pending five years should be carefully studied by the supervisory patent examiner and every effort should be made to terminate its prosecution. In order to accomplish this result, the application is to be considered "special" by the examiner.

The present application thus has a "special" status under M.P.E.P. § 707.02 and should be processed accordingly.

5. Withdrawn Objections and Rejections

Rejections and objections not reiterated are withdrawn. *See* 37 C.F.R. § 1.113(b); M.P.E.P. §§ 706.07 and 707.07(e).

6. Rejection Under 35 U.S.C. § 112, Second Paragraph (Indefiniteness)

The Office rejects claims 17-31 and 47-48 under 35 U.S.C. § 112, second paragraph, as allegedly indefinite. Office Action, page 3. The recitation of "in need thereof" is allegedly unclear as to in need of (1) treating liver diseases associated with hepatopathy or (2) taking the omega-9 unsaturated fatty acid. *Id.*

As amended, independent claims 17 and 24 no longer recite "in need thereof." Instead, amended claims 17 and 24 recite *inter alia* that "the subject is a patient having a disease associated with hepatopathy." The Office's rejection is thus mooted. Claims 22-23 and 29-30 are canceled, mooting the rejection. Applicants respectfully request withdrawal of the rejection, and allowance of the claims.

7. Rejection Under 35 U.S.C. § 112, First Paragraph (Enablement)

Grounds For Rejection

The Office rejects claims 17-31 and 47-48 under 35 U.S.C. § 112, first paragraph, as allegedly failing to comply with the enablement requirement. Office Action, pages 3 and 7-8. The complex nature of the claims allegedly is "greatly exacerbated" by the breadth of the claims. *Id.*, at 3. The Specification allegedly fails to provide guidance to enable "the full scope of the

claimed invention based on the effects of a specific omega-9 fatty acid composition." *Id.*, at 3-4. The hepatopathy model induced by GalN/LPS treatment is allegedly not predictive of treating the recited diseases. *Id.*, at 4. The Office also alleges that "it is not readily apparent that the prior art recognized methods" of treating the claimed diseases "with the presently claimed compound at the time of the invention...such that one of ordinary skilled in the art would have been able to drawn upon the knowledge already present in the prior art to execute the treatment of" of the claimed diseases. *Id.*, at 5-6. The Specification allegedly (1) "failed to provide any clear correlation of such disclosed general procedure to the instantly claimed compound"; and (2) "failed to provide any working or prophetic examples directed to a possible method and/or manner of treating" the claimed diseases. *Id.*, at 6. The Office admits that the Specification is enabled for obtaining a fatty acid by culturing *Mortierella alpina* mutant strains SAM 1861 and SAM 2086. *Id.*, at 7-8. However, the Office alleges that the Specification fails to provide enablement for obtaining fatty acids from microorganisms recited in claims 21 and 28. *Id.*, at 8.

Arguments

Applicants traverse the rejection to the extent it may be applied to the amended claims. First, the Office mischaracterizes the claimed methods. To justify the complex nature of the claims, the Office alleges, "[t]he claims encompass the use of ***compound of formula I***, but fail to show how these fatty acids...are used for ameliorating liver diseases associated with hepatopathy." *Id.*, at 4 (emphasis added). Applicants submit that (1) "compound of formula I" could not be located throughout the Specification or in the present claims; and (2) Examples 1-3, spanning pages 18-19 of the Specification, describe administering omega-9 fatty acid-containing compositions to significantly suppress hepatopathy in mice treated with GalN/LPS. Thus, the Office's lack of enablement allegations are unsupported. Reconsideration in view of the above clarification is respectfully requested.

Second, the Office has not provided any ***objective evidence or reasoning*** why the presently claimed processes are not enabled, or a rationale of why the claimed processes would not work. *See In re Cortright*, 165 F.3d 1353, 1357, 49 U.S.P.Q.2d 1464, 1466 (Fed. Cir. 1999). In the present case, the Office, without providing any reasoning or rationale, asserts that the GalN/LPS-induced hepatopathy model in mice is not predictive of treating the recited diseases.

Applicants submit that "it is incumbent upon the Patent Office ... to explain why it doubts the truth or accuracy of any statement in a supporting disclosure and to back up assertions of its own with acceptable evidence or reasoning which is inconsistent with the contested statement." *See In re Marzocchi*, 439 F.2d 220, 224, 169 U.S.P.Q. 367, 370 (C.C.P.A. 1971). Thus, the Office has not brought forward any evidence supporting lack of enablement.

Third, the Office's allegation as to the GalN/LPS mice model is unsubstantiated. Applicants note that correlation between an actual disease condition and an animal model must be determined from the perspective of one skilled in the art—not based on the unsupported conjecture or opinion. *In vitro* and *in vivo* models disclosed in an application constitute ***working examples*** of the invention, provided ***the models "correlate" with the claimed method.*** The relevant legal standard that the Office must apply is set forth in the Manual of Patent Examining Procedure (M.P.E.P.), § 2164.02, "Working Example," 8th ed., revised Sept. 2007. This section sets forth two key requirements of the Office's reviewing Court. [1] Additionally, only a reasonable correlation is required—not a rigorous or an invariable exact correlation. *See e.g., In re Brana*, 51 F.3d 1560, 1566, 34 U.S.P.Q.2d 1436, 1441 (Fed. Cir. 1995); *Cross v. Iizuka*, 753 F.2d 1040, 1050, 224 U.S.P.Q. 739, 747 (Fed. Cir. 1985). The Office fails to provide ***any*** evidence as to why the mice model described in the Specification is not predictive or correlative to the claimed diseases associated with hepatopathy. Applicants submit that GalN/LPS treated

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[1] **CORRELATION: *IN VITRO/IN VIVO***

The issue of "correlation" is related to the issue of the presence or absence of working examples. "Correlation" as used herein refers to the relationship between *in vitro* or *in vivo* animal model assays and a disclosed or a claimed method of use. An *in vitro* or *in vivo* animal model example in the specification, in effect, constitutes a "working example" if that example "correlates" with a disclosed or claimed method invention. If there is no correlation, then the examples do not constitute "working examples." In this regard, the issue of "correlation" is also dependent on the state of the prior art. In other words, if the art is such that a particular model is recognized as correlating to a specific condition, then it should be accepted as correlating unless the examiner has evidence that the model does not correlate. Even with such evidence, the examiner must weigh the evidence for and against correlation and decide ***whether one skilled in the art*** would accept the model as reasonably correlating to the condition. *In re Brana*, 51 F.3d 1560, 1566, 34 USPQ2d 1436, 1441 (Fed. Cir. 1995) (reversing the PTO decision based on finding that *in vitro* data did not support *in vivo* applications).

Since the initial burden is on the examiner to give reasons for the lack of enablement, the examiner must also give reasons for a conclusion of lack of correlation for an *in vitro* or *in vivo* animal model example. ***A rigorous or an invariable exact correlation is not required***, as stated in *Cross v. Iizuka*, 753 F.2d 1040, 1050, 224 USPQ 739, 747 (Fed. Cir. 1985):

> [B]ased upon the relevant evidence as a whole, there is a ***reasonable correlation*** between the disclosed *in vitro* utility and an *in vivo* activity, and therefore a rigorous correlation is not

mice are widely used to study hepatocyte destruction. *See, e.g.*, Leist et al., 146 AM. J. PATHOL. 1220 (1995) (enclosed as **EXHIBIT I**). Accordingly, there is at least a reasonable correlation between the described GalN/LPS model and the claimed diseases. The Office's reconsideration in view of the above arguments is respectfully requested.

Fourth, Applicants submit that the Office assertion as to the guidance and recognized methods from the prior art[2] is unsupported. The present inventors have newly discovered that administering omega-9 fatty acids ameliorates the recited diseases associated with hepatopathy. There cannot be any recognition or guidance in the prior art as to the claimed methods, when the claimed methods are novel.

Finally, the Specification enables obtaining omega-9 fatty acids from the recited microorganisms. As the Office admits, the Specification provides working examples wherein omega-9 fatty acids are obtained from *Mortierella alpina* strains. The Office is respectfully directed to **Kawashima** et al., U.S. Patent No. 5,322,780 (issued June 21, 1994) ("Kawashima"). Kawashima describes that omega-9 fatty acids can be obtained from various microorganisms. *See, e.g.*, col. 2, ln. 40 to col. 5, ln. 44 (describing the procedure of generating omega-9 fatty acid-producing microorganisms other than *Mortierella*, as well as culturing the microorganisms and recovering the omega-9 fatty acid-containing composition). Given the knowledge in the art at the time of the invention, the degree of exemplification reasonably correlates with the scope of the claims in the present case. Applicants note that exemplification of each and every embodiment encompassed by a claim is not required to comply with the enablement requirement even in an unpredictable art. *See e.g.*, *In re Angstadt*, 537 F.2d 498, 502-503, 190 U.S.P.Q. 214, 218 (C.C.P.A. 1976).

Given at least these arguments, the Office has failed to adduce a *prima facie* argument for lack of enablement. Claims 22-23 and 29-30 are canceled, mooting the rejection.

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necessary where the disclosure of pharmacological activity is reasonable based upon the probative evidence. (Citations omitted.)

[2] "In addition, it is not readily apparent that the prior art recognized methods of treating acute or chronic hepatitis, acute hepatic insufficiency, liver cirrhosis, and/or hepatoma with the presently claimed compound at the time of the invention (or at least Applicant has failed to point to such information in a document that can be properly incorporated by reference) such that one of ordinary skill in the art would have been able to drawn upon the knowledge already present in the prior art to execute the treatment of acute or chronic hepatitis, acute hepatic

Accordingly, Applicants respectfully request withdrawal of the rejection and allowance of the claims.

8. Rejection Under 35 U.S.C. § 112, First Paragraph (Written Description)

Grounds For Rejection

The Office rejects claims 17-31 and 47-48 under 35 U.S.C. § 112, first paragraph, as allegedly failing to comply with the written description requirement. Office Action, page 12. The recitation of "a compound having an omega-9 unsaturated fatty acid as a constituent fatty acid" allegedly lacks chemical structural information. *Id.* The Office also alleges that "[t]he species specifically disclosed are not representative of the genus because the genus is highly varia[ble]." *Id.*, at 14.

Arguments

Applicants traverse the rejection to the extent it may be applied to the amended claims. Whether generic claims to biological subject matter comply with the written description requirement is determined by an analysis of the *Capon* factors: (1) the existing knowledge in the particular field, (2) the extent and content of the prior art, (3) the maturity of the science or technology, (4) the predictability of the subject matter at issue, and (5) other considerations appropriate to the subject matter. *See Capon v. Eshhar*, 418 F.3d 1349, 1358, 76 U.S.P.Q.2d 1078, 1085 (Fed. Cir. 2005); *see also Ariad Pharmaceuticals Inc. v. Eli Lilly & Co.*, 598 F.3d 1336, 1351, 94 U.S.P.Q.2d 1161, 1172 (Fed. Cir. 2010) (*en banc*) (citing *Capon* with approval). In the present rejection, the Office has failed to perform an analysis of the above factors. Thus, no *prima facie* argument for lack of written description has been adduced.

Applicants note that the Specification provides multiple working examples of the claimed compounds. For example, the Specification provides a laundry list of the claimed "compound having an omega-9 unsaturated fatty acid as a constituent fatty acid." *See,* Specification, first full paragraph at page 4. The Federal Circuit explicitly holds that working examples covering the full scope of the claims are not required for an adequate written description. *See e.g.*,

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insufficiency, liver cirrhosis, and /or hepatoma with the presently claimed compound absent factual evidence to the contrary." Office Action, paragraph bridging pages 5-6.

Falkner v. Inglis, 448 F.3d 1357, 1366, 79 U.S.P.Q.2d 1001, 1007 (Fed. Cir. 2006);[3] *see also Ariad* at 598 F.3d 1336, 1352, 94 U.S.P.Q.2d at 1172.[4] The Office's allegation as to lack of chemical structure would necessarily require Applicants to provide working examples covering the full scope of the claims. This requirement directly contradicts the established law.

Given at least these arguments, claims as amended comply with the written description requirement. Claims 22-23 and 29-30 are canceled, mooting the rejection. Accordingly, Applicants respectfully request withdrawal of the rejection and allowance of the claims.

9. Obviousness-Type Double Patenting Rejection

Grounds For Rejection

The Office rejects claims 17-20, 22-27, 29-31, and 47-48 under the judicially created doctrine of obviousness-type double patenting as allegedly unpatentable over claims 1-3, 5-6, and 9 of **Akimoto** et al., U.S. Patent No. 5,981,588 ("Akimoto").[5] Office Action, page 15. Claims of Akimoto allegedly recite administering an omega-9 unsaturated fatty acid to prevent or alleviate medical symptoms caused by delayed allergic reactions. *Id.* The medical symptom allegedly may include hepatitis. *Id.* The Office concludes that the subject matter of the present claims is not considered to be patentably distinct, because it allegedly conflicts with the subject matter claimed in Akimoto. *Id.*

Arguments

Applicants traverse the rejection to the extent it may be applied to the amended claims. The requirement for patentable distinction in an obviousness-type double patenting rejection is

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[3] "A claim will not be invalidated on section 112 grounds simply because the embodiments of the specification do not contain examples explicitly covering the full scope of the claim language. That is because the patent specification is written for a person of skill in the art, and such a person comes to the patent with the knowledge of what has come before."

[4] "We have made clear that the written description requirement does not demand either examples or an actual reduction to practice; a constructive reduction to practice that in a definite way identifies the claimed invention can satisfy the written description requirement."

[5] The Office alleges, "claim 17-20, 22-27, 29-31, and 47-48 are not considered to be patentably distinct over claims 1-3, 5, 6, and 9 of ***U.S. Patent No. 6685953 B1***, and are properly rejected under the judicially created doctrine of obviousness-type double patenting as being obvious and unpatentable variants." Office Action, page 15 (emphasis added). Applicants note that U.S. Patent No. 6,685,953 (1) has only five claims and (2) relates to a diamide derivative. Accordingly, the Examiner must have meant that the double patent rejection is over claims of U.S. Patent No. 5,981,588 instead.

"analogous to the non-obviousness requirement of 35 U.S.C. 103," except that the patent principally underlying the double patenting rejection is not considered prior art. *See* M.P.E.P. § 804(II)(B)(1). A finding of obviousness under 35 U.S.C. § 103 requires that both the suggestion of the claimed invention and the expectation of success must be in the prior art, not in the disclosure of the claimed invention. *In re Dow Chem. Co.*, 837 F.2d 469, 5 U.S.P.Q.2d 1529 (Fed. Cir. 1988). Additionally, "obviousness requires a suggestion of ***all*** limitations in a claim." *CFMT, Inc. v. Yieldup Int'l Corp.*, 349 F.3d 1333, 1342, 68 U.S.P.Q.2d 1940, 1947 (Fed. Cir. 2003) (emphasis added).

Amended claims 17 and 24 recite, *inter alia*, that "the liver diseases associated with hepatopathy are acute hepatic insufficiency, liver cirrhosis and/or hepatoma." Applicants submit that the recited liver diseases differ from the claimed medical symptoms of Akimoto. The claimed medical symptoms of Akimoto are caused by delayed allergic reactions. There is no evidence on the record that delayed allergic reactions could cause "acute hepatic insufficiency, liver cirrhosis and/or hepatoma." Thus, amended claims 17 and 24, as well as the dependent claims 18-20, 25-27, 31, and 47-48, are patentably distinct from claims 1-3, 5-6, and 9 of Akimoto. Claims 22-23 and 29-30 are canceled, mooting the rejection. Applicants respectfully request withdrawal of the rejection and allowance of the claims.

10. Rejection Under 35 U.S.C. § 103

Grounds For Rejection

The Office rejects claims 17-31 and 47-48 under 35 U.S.C. § 103(a) as allegedly obvious over Akimoto. Office Action, page 16. Akimoto allegedly teaches a method for preventing or alleviating medical symptoms caused by delayed allergic reactions by administering an omega-9 unsaturated fatty acid. *Id.* Akimoto also allegedly teaches that the medical symptom resulted from a delayed allergic reaction may include hepatitis. *Id.*, at 17. The Office alleges that it "would have been obvious to have used Akimoto et al. to produce a method of ameliorating liver diseases administering omega-9 unsaturated fatty acid." *Id.* The Office further alleges that the Akimoto teaches "the same composition and method with the same mechanism and overlapping dosage range to be used for the same purpose as the claimed invention." *Id.*

Arguments

Applicants traverse the rejection to the extent it may be applied to the amended claims. Amended claims 17 and 24 recite, *inter alia*, that "the liver diseases associated with hepatopathy are acute hepatic insufficiency, liver cirrhosis and/or hepatoma." Applicants submit that the recited liver diseases differ from the claimed medical symptoms of Akimoto. The claimed medical symptoms of Akimoto are caused by delayed allergic reactions. There is no evidence on the record that delayed allergic reactions could cause "acute hepatic insufficiency, liver cirrhosis and/or hepatoma." The Office also fails to provide evidence that a skilled artisan would have been directed to treating the claimed diseases with a method that treats symptoms caused by delayed allergic reactions. Thus, Akimoto at least fails to teach ameliorating the recited diseases. Without all claim elements taught, there can be no expectation that the presently claimed method would have worked predictably.

Given at least these arguments, amended claims 17 and 24 are nonobvious over Akimoto. Dependent claims 18-21, 26-28, 31, and 47-48 are likewise nonobvious for at least the same reasons. Claims 22-23 and 29-30 are canceled, mooting the rejection. Accordingly, Applicants respectfully request withdrawal of the rejection and allowance of the claims.

CONCLUSION

In view of the above arguments and amendments to the claims, Applicant submits that the claims are in condition for allowance and respectfully request reconsideration and timely allowance of the claims.

Should the Office have any questions or comments regarding Applicant's amendments or response, please contact Applicant's undersigned representative at (202) 230-5119. Furthermore, please direct all correspondence to the below-listed address.

In the event that the Office believes that there are fees outstanding in the above-referenced matter and for purposes of maintaining pendency of the application, or for Notice of Appeal, the Office is authorized to charge the outstanding fees to Deposit Account No. 50-0573. The Office is likewise authorized to credit any overpayment to the same Deposit Account Number.

Respectfully Submitted,

Date: October 21, 2011 By: _____

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